AMENDMENT

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application. Please cancel claims 17 and 51. Please amend claims 1-16, 18-21, 24, 42-43, 45-47, 49 and 52-56 as set forth below. Please add new claims 59-60.

LISTING OF CLAIMS

1. (**Currently amended**) ~~Use of a composition comprising substances contained in *Cimicifuga Racemosa* extract, or derivatives thereof, which induces a physiological estrogen like effect without interacting with breast cancer cells, for the preparation of a medicament for the treatment of~~ A method of treating an estrogen deficiency symptom or disease of a mammal suffering from or having a high risk of developing breast cancer, comprising administering to a mammal suffering from or having a high risk of developing breast cancer a composition comprising an admixture of an extract of *Cimicifuga racemosa* or derivatives thereof, and a pharmaceutically-acceptable carrier, which induces a physiological estrogen-like effect without interacting with breast cancer cells.

2. (**Currently amended**) ~~Use~~ A method according to claim 1, wherein the composition ~~which~~ induces a physiological estrogen-like effect without stimulating breast cancer cells.

3. (**Currently amended**) ~~Use~~ A method according to claim 1, wherein the physiological estrogen-like effect is uterine growth as determined by an increase in uterine weight compared to controls after administration of the composition to ovariectomized female athymic nude mice.

4. (**Currently amended**) ~~Use~~ A method according to claim 1, wherein the physiological estrogen-like effect is uterine growth as determined by an increase in mean uterine weight compared to controls of at least 0.10 g after administration of the composition to ovariectomized NMRI female athymic nude mice for 8 days.

5. (**Currently amended**) ~~Use~~ A method according to claims 3 or 4, wherein the increase in uterine weight obtained by administration of a dose comparable to a normal dose

for the mammal to be treated ~~of~~ with the composition corresponds to a weight increase obtainable in the same test animal by estradiol treatment.

6. **(Currently amended)** ~~Use~~ A method according to any of claims 3 or 4, wherein the increase in uterine weight obtained by administration of a dose comparable to a normal dose for the mammal to be treated of the composition corresponds to a substantially maximum weight increase obtainable in the same test animal by estrogen treatment.

7. **(Currently amended)** ~~Use~~ A method according to claim 1, wherein the physiological estrogen-like effect is a change in gonadotropins (FSH and/or LH) as determined by available validated radioimmuno assay techniques.

8. **(Currently amended)** ~~Use~~ A method according to claim 1, wherein the physiological estrogen-like effect is a change in cytology of the vaginal cells as determined by cytological counts.

9. **(Currently amended)** ~~Use~~ A method according to claim 1, wherein the composition does not interact with cancer cells that are estrogen receptor-negative.

10. **(Currently amended)** ~~Use~~ A method according to claim 1, wherein the lack of interaction with breast cancer cells is determined by no effect of the composition as compared to a control on growth of the estrogen and progesterone receptor negative MDA-MB-231 (ATCC HTB-26) human breast cancer cell line inoculated into six-week-old female athymic nude mice determined when control tumours show increasing size during at least six consecutive growth recordings.

11. **(Currently amended)** ~~Use~~ A method according to claim 1, wherein the composition does not interact with cancer cells that are estrogen receptor-positive.

12. **(Currently amended)** ~~Use~~ A method according to claim 1, wherein the lack of interaction with breast cancer cells is determined by no effect of the composition compared to a control on growth of the estrogen dependent and estrogen receptor-positive MCF-7 (ATCC HTB-22) human breast cancer cell line inoculated into six-week-old female athymic nude mice determined when control tumours show increasing size during at least six consecutive growth recordings.

13. (**Currently amended**) ~~Use~~ A method according to claim 1, wherein the lack of interaction with breast cancer cells is determined by no effect of the composition when given in combination with estradiol compared to a control on growth of the estrogen dependent and estrogen receptor-positive MCF-7 (ATCC HTB-22) human breast cancer cell line inoculated into six-week-old female athymic nude mice determined when control tumours show increasing size during at least six consecutive growth recordings.

14. (**Currently amended**) ~~Use~~ A method according to claim 1 for the treatment of estrogen deficiency symptoms or diseases of humans having breast cancer~~,~~ or having a high risk of recurrent breast cancer~~, or having a risk of developing breast cancer~~.

15. (**Currently amended**) ~~Use~~ A method according to claim 1, wherein the estrogen deficiency symptom or disease includes a menopausal symptom; a dermatological disorder; dryness of mucous membranes; a brain related disease; a bone or joint related disease; vaginal estrogen deficiency; a coronary heart disease; hyperlipidaemia; ~~and~~ hypercholesterolaemia; or arteriosclerosis.

16. (**Currently amended**) ~~Use~~ A method according to claim 1, wherein the estrogen deficiency symptom is a menopausal symptom.

17. Canceled.

18. (**Currently amended**) ~~Use~~ A method according to claim 1, wherein the composition is a composition comprising *Cimicifuga ~~R~~racemosa* plant parts.

19. (**Currently amended**) ~~Use~~ A method according to claim 1, wherein the composition is a composition comprising SPP-001.

20. (**Currently amended**) ~~Use~~ A method according to claim 1, wherein the composition is a composition comprising one or more chemical compounds contained in *Cimicifuga ~~R~~racemosa* extract, or derivatives thereof.

21. (**Currently amended**) ~~Use~~ A method according to claim 1, wherein the composition is combined with a drug which has a selective estrogen receptor modulating (SERM) activity.

22. (Previously presented) A container comprising a composition according to claim 1 with a pharmaceutical carrier and comprising an indication for relief of an estrogen deficiency symptom without increasing the risk of developing or worsening estrogen dependent cancer.

23. (Previously presented) A container comprising a composition which induces a physiological estrogen-like effect without stimulating breast cancer cells, a pharmaceutical carrier and further comprising an indication for relief of estrogen deficiency symptoms without increasing the risk of developing or worsening estrogen dependent cancer.

24. (**Currently amended**) A method for relieving symptoms caused by estrogen deficiency in a mammal suffering from or having a high risk of developing an estrogen dependent tumour comprising administering to the mammal a composition comprising substances contained in *Cimicifuga ~~R~~racemosa* extract, or derivatives thereof, which induces a physiological estrogen-like effect without stimulating breast cancer cells.

25. (Previously presented) A method according to claim 24, wherein the mammal is a human.

26. (Previously presented) A method for screening for substances or compositions which can be used according to claim 1 or 2, comprising subjecting substances or compositions to

1) testing for possible estrogen-like effect in normal tissue by measuring increase in uterine weight, changes in gonadotropins, changes in vaginal cytology, postmenopausal symptoms or a combination thereof in an adult female mammal, and

2) testing for possible estrogenic effect in breast cancer, and selecting, as candidates for tissue-selective estrogenic substances or compositions useful in the method according to claim 1 or 2, substances or compositions which,

    a) are capable of inducing physiological estrogenic effects in female mammals, and at the same time

b) have no effect on the growth of estrogen receptor-negative cancer cells and no effect on estrogen receptor-positive cancer cells in the doses in which they induce physiological estrogen effects.

27. (Previously presented) A method according to claim 26, wherein the capability of the substance or composition of inducing physiological estrogen effects is tested by testing the capability of the substance or composition of effecting uterine weight increase in ovariectomized female NMRI athymic nude mice, the lack of effect of the substance or composition on the growth of estrogen receptor-negative cancer cells is assessed as the lack of capability of the substance or composition of supporting growth of MDA-MB231 xenografts in female NMRI athymic nude mice, and the lack of effect of the substance or composition on the growth of estrogen receptor-positive cancer cells is assessed as the lack of capability of the substance or composition of supporting growth of MCF-7 (ATCC (HTB-22) xenografts in female NMRI athymic nude mice.

28. (Previously presented) A method for relieving or curing symptoms or diseases which are caused by estrogen deficiency, or which can be relieved or cured by administration of steroidal estrogen, in a mammal who suffers from breast cancer, or has a risk of recurrent breast cancer, or has a high risk of developing breast cancer, the method comprising administering, to the mammal, a composition which has an estrogen-like effect, as evidenced by a capability of the composition of inducing physiological estrogenic effects in adult mammal, and which is free from interaction with breast cancer cells, thereby treating estrogen deficiency symptoms or diseases without introducing a risk of provoking the development of clinically evident breast cancer, stimulating growth of existing breast cancer cells in the mammal or a combination thereof.

29. (Previously presented) A method according to claim 28, wherein the mammal is a female mammal.

30. (Previously presented) A method according to claim 29, wherein the female mammal is a woman.

31. (Previously presented) A method according to claim 29, wherein the estrogen-like effect possessed by the composition manifests itself in the composition being capable of

inducing an increase in uterine weight in adult ovariectomized NMRI female athymic nude mice.

32. (Previously presented) A method according to claim 31, wherein the increase in uterine weight following a dose comparable to a normal dose for the mammal to be treated corresponds to a weight increase seen in the same test animal following estradiol treatment.

33. (Previously presented) A method according to claim 32, wherein the increase in uterine weight following a dose comparable to a normal dose for the mammal to be treated corresponds to a substantially maximum weight increase obtainable in the same test animal by estrogen treatment.

34. (Previously presented) A method according to claim 28, wherein the estrogen-like effect possessed by the composition manifests itself in the composition being capable of inducing a lowering in FSH and LH in females.

35. (Previously presented) A method according to any of claims 30-34, wherein the estrogen-like effect possessed by the composition manifests itself in the composition being capable of inducing an estrogen like change in vaginal cytology in females.

36. (Previously presented) A method according to claim 28, wherein the composition is one which has no effect on the growth of estrogen receptor-negative cancer cells.

37. (Previously presented) A method according to claim 36, wherein the composition is one which has no effect on the growth of xenografts of the estrogen and progesteron receptor-negative MDA-MB-231 (ATCC HTB-26) human breast cancer cell line in nude mice.

38. (Previously presented) A method according to claim 28, wherein the composition is one which is free from any effect on breast cancer cells even where the breast cancer cells are documented as being estrogen receptor-positive.

39. (Previously presented) A method according to claim 28, wherein the composition is one which has substantially no agonizing and substantially no antagonizing

effect on the effect of estrogen on breast cancer cells, even where the breast cancer cells are documented as being estrogen receptor-positive.

40. (Previously presented) A method according to claim 39, wherein the composition is one which substantially does not bind to estrogen receptors of cancer cells.

41. (Previously presented) A method according to claim 38, wherein the composition is one which has no effect on xenografts of the estrogen receptor-positive and estrogen dependent MCF-7 (ATCC HTB-22) human breast cancer cell line in nude mice, as evidenced by the composition having no growth supportive effect and no growth inhibitory effect on the xenografts whether given alone or in combination with estradiol.

42. **(Currently amended)** A method according to claim 41, wherein the composition is one which has no effect on xenografts of the estrogen receptor-positive and estrogen dependent MCF-7 (ATCC HTB-22) human breast cancer cell line in nude mice, as evidenced by the composition having no growth supportive effect and no growth inhibitory effect on the xenografts whether given alone or in combination with estradiol, even where the composition is ~~ad-ministered~~ administered in a dose which is 10 times higher than a dose giving, in the same strain of nude mice, a maximum uterus weight increase.

43. **(Currently amended)** A method according to claim 28, wherein the estrogen deficiency-conditioned symptom or disease includes a menopausal symptom, a dermatological disorder, dryness of mucous membranes, a brain related disease, a bone and joint related disease, vaginal estrogen deficiency, a coronary heart disease, hyperlipidaemia, hypercholesterolaemia, ~~and~~or arteriosclerosis.

44. (Previously presented) A method according to claim 43, wherein the estrogen deficiency-conditioned symptoms are menopausal symptoms.

45. **(Currently amended)** A method according to claims 28 or 43, wherein the composition is a composition comprising substances included in *Cimicifuga ~~R~~racemosa* extract, or derivatives thereof.

46. **(Currently amended)** A method according to claim 45, wherein the composition is or includes a *Cimicifuga ~~R~~racemosa* extract.

47. **(Currently amended)** A method according to claim 45, wherein the composition is a composition comprising *Cimicfuga ~~R~~racemosa* plant parts.

48. (Previously presented) A method according to claim 45, wherein the composition is a composition comprising SPP-001.

49. **(Currently amended)** A method according to claim 46, wherein the composition is a composition comprising one or more chemical compounds included in *Cimicifuga ~~R~~racemosa* extract, or derivatives thereof.

50. (Previously presented) A method according to claim 28, wherein the composition is combined with a drug which has a selective estrogen receptor modulating (SERM) activity.

51. Canceled.

52. **(Currently amended)** ~~Use~~ A method according to claim 9, wherein the composition does not stimulate cancer cells that are estrogen receptor-negative.

53. **(Currently amended)** ~~Use~~ A method according to claim 10, wherein the lack of interaction with breast cancer cells is lack of stimulation of breast cancer cells.

54. **(Currently amended)** ~~Use~~ A method according to claim 11, wherein the composition does not stimulate cancer cells that are estrogen receptor-positive.

55. **(Currently amended)** ~~Use~~ A method according to claim 12, wherein the lack of interaction is lack of stimulation of breast cancer cells.

56. **(Currently amended)** ~~Use~~ A method according to claim 13, wherein the lack of interaction is lack of stimulation of breast cancer cells.

57. (Previously presented) A method according to claim 28, wherein the composition is free from a stimulating effect on breast cancer.

58. (Previously presented) A method according to claim 39, wherein the composition has substantially no agonizing and substantially no antagonizing effect on the effect of estradiol on breast cancer cells.

59. **(New)** A method according to claim 1, wherein the mammal is a female mammal.

60. **(New)** A method according to claim 59, wherein the female mammal is a woman